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14. ABSTRACT
This report covers progress completed on "Biomarkers for PTSD" from 6/3/09-6/2/10. During this period the grant has been transferred from NCIRE to New York University School of Medicine (NYUMC), where the PI, Dr. Marmar, has taken a position as Chair of Psychiatry. This study is in the start-up phase, and major goals have included getting IRB approvals, hiring study personnel, and optimizing procedure manuals for handling of samples and patient data. Major progress has been made on each of these fronts. Because this is a complex and large multi-site study, a significant portion of time must be devoted to project start-up.

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INTRODUCTION:

It is estimated that 10% to 20% (1-4) of warfighters who have served in Iraq and Afghanistan have PTSD. An important limitation of these estimates is the reliance on self-report screening measures and clinical interviews to make the diagnosis of PTSD. These methods are subject to a number of biases, including underreporting of PTSD symptoms because of stigma of mental illness and concerns about adverse effects on careers, and exaggeration of symptoms in those seeking compensation for service- connected disability (5). Development of biomarkers of PTSD is critical for DOD and VA as objective indicators of PTSD for use in post-deployment medical screening, treatment selection, treatment outcome monitoring, disability evaluations, and for informing novel targets for treatment development. Additionally, biomarkers hold great potential for explaining and mitigating the associations between war zone-related PTSD and physical health problems, including cardiovascular and metabolic disorders (6-10). In order to address this critical gap we will perform a pilot study to determine feasibility for larger scale biomarker identification and biomarker informed intervention studies by carefully examining 200 OIF/OEF warfighters through an extensive biological protocol. The first phase will pilot the integration of methods across five leading research laboratories and identify the most promising biomarkers in preparation for larger scale studies. Given the sample size for the pilot and large number of biomarkers of interest, we will specify a limited set of biomarkers for hypothesis testing. It is predicted that compared with controls the PTSD group will have smaller dentate/CA3 hippocampal subfield volumes, lower ambient cortisol levels, and greater cortisol suppression following dexamethasone administration. It is also predicted that lower neuropeptide Y levels will be associated with smaller Dentate/CA3 volumes, and that APO E4 polymorphisms will be associated with smaller Dentate/CA3 volumes.

BODY:

According to the Statement of Work, the goal of the initial start-up phase of this study was to focus on gaining regulatory approval,hiring staff, and preparing the study for launch.

In December of 2009 Dr. Marmar transitioned to a new position as Chair of the Department of Psychiatry at New York University Medical Center (NYUMC). Hence, the effort and focus has been on relinquishment of this grant from the DOD and Northern California Institute for Research and Education (NCIRE) and the transfer of this grant to NYU. The paperwork for this process was completed in 2010. The process to transfer this grant entailed several meetings with NCIRE and NYU contracts and grants specialists, reworking the budget and budget justification for NYU and resubmitting all documentation to NYU and the DOD for approval of the transfer of this grant. In addition, weekly conference calls among the multi-site personnel have been held to develop the infrastructure and coordination of this highly complex study. During the meetings we also worked through details to establish the budgets, determine the personnel needs, and to develop procedures for IRB submission at the multi-sites.

The IRB protocol has undergone several rounds of amendments in order to coordinate changes requested amongst the multiple institutions involved in the study and the DOD, as well as changes to accommodate requests for blood samples and data sharing from the basic science groups at Walter Reed, University of California at Santa Barbara, and the Institute of Systems Biology, who are involved in the larger collaborative effort that aims to apply a systems biology approach to PTSD. A final version of this protocol has now been approved by the parent IRB at NYU. This version of the protocol is now under review at the collaborating institutes (MSSM, JJPVAMC, and UCSF) with approval expected in September. Full approval has been received by the UCSF/SFVAMC neuroimaging site, which will solely be analyzing de-identified imaging data.

A federal certificate has been obtained.

Recruitment materials have been developed at the parent site and shared with the other recruitment sites (JJPVAMC/MSSM). A recruitment plan has been developed to coordinate efforts between these sites. A recruiter was hired, who has been contacting veteran organizations, VAs, and CBOCs within the boroughs of New York City, which will be the focus of recruitment efforts.

A Research Assistant was hired. The Research Assistant has begun preparing interview and self-report materials and manualizing procedures, which will be standardized across sites.

Neuroimaging piloting has been underway. Five healthy volunteer pilot participants were run on the imaging protocol at NYU's Center for Biomedical Engineering. Images were sent to UCSF/SFVAMC. The image processing team at UCSF/SFVAMC has been working with the NYU team to work out signal-to-noise issues in data acquisition, to finalize parameters, and to finalize procedures for sharing of data.

A database manager was hired to begin developing the database for this study. A data sharing agreement was approved to share data between the JJPVAMC and NYU

KEY RESEARCH ACCOMPLISHMENTS:

- Transfer of grants from NCIRE to NYU due to move of PI, Charles Marmar, M.D., to NYU as Chair of the Department of Psychiatry was completed on March 18, 2010
- Hiring: Recruiter, Research Assistant, Database Manager
- Developed recruitment materials, prepared clinical and self-report materials by organizing into a single packet, began manualizing procedures for standardization across sites.
- Began neuroimaging pilot to finalize imaging parameters, protocols and sharing procedures.
- IRB: obtained final IRB approval at:
    - at the parent site: NYU
    - The neuroimaging core at the San Francisco VA: An expedited modification to a "databank" protocol, in use by the neuroimaging processing core at the San Francisco VA, was made to add Dr. Marmar's study to their list of laboratories from whom they receive de-identified imaging data for processing
    - IRB approvals for each of the additional cores are underway
        - At the 2 additional recruitment sites: Bronx VA and Mount Sinai School of Medicine
        - At UCSF, where de-identified biological samples will be analyzed

REPORTABLE OUTCOMES:

The major development during this phase of project start-up has been in developing the study infrastructure, hiring personnel, and preparing for study launch, which is expected in early August. Because of the complexity of this study and the number of institutions involved, including the larger collaborative effort with the basic science researchers, gaining IRB approvals have been a major focus of the start-up effort. Now that the protocol is finalized, we are expecting full approvals to be obtained from remaining institutions by mid to late September.

Tasks to complete include: (1) hiring and training additional personnel to work on this project, i.e., project coordinator and clinical interviewer; (2) obtain IRB approval at all sites and the DOD; (3) finish manualizing the procedures across sites; (4) develop a highly complex data management system between and among sites; (5) and begin running study participants late September (pending DOD final IRB approval)..

CONCLUSION: The study has received IRB approval from NYUMC, the new administrative core of this multisite study since Dr. Marmar's move in December. IRB applications have also been submitted to the other two recruitment sites: the James J Peters VAMC (JJPVAMC) and Mount Sinai School of Medicine (MSSM). The JJPVAMC application is undergoing its second round of reviews, and the MSSM application was just submitted. Expedited applications will be submitted to 2 sites that will be processing de-identified blood, urine, and neuroimaging data: University of California, San Francisco and San Francisco VA. Staff has been hired in New York, including a research assistant, project coordinator, and two post-docs.

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